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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,011	07/23/2001	Mark Leslie Smythe	065064/0135	9310

7590

12/17/2002

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EXAMINER

CLOW, LORI A

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 12/17/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,011

Applicant(s)

SMYTHE ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 and 27-30 is/are pending in the application.
- 4a) Of the above claim(s) 20-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 and 27-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6. 6) ☐ Other: _____

DETAILED ACTION

Applicant's election of Group I, claims 1-19 and 27-30 in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-19 and 27-30 are pending. Claims 20-26 have been withdrawn, as directed to non-elected claims.

Drawings

Applicant is hereby notified that the required timing for the correction of drawings has changed. See the last 6 lines on the sheet which is attached entitled "Attachment for PTO-948 (Rev. 03/01 or earlier)". Due to the above notification Applicant is required to submit drawing corrections within the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

Claim Rejections - 35 USC § 112

Claims 1-30 are rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to engineer a protein. The claims set forth query sequence comparisons. For the reasons discussed below, this constitutes undue experimentation.

b) and c) The specification provides examples of identifying framework proteins suitable for further modification by matching and comparing query protein sequence to known database sequences (pages 21). However, nowhere in the specification are proteins engineered using this method. At best, proteins are queried to find structural similarities so that a particular protein can further be modified.

d) The invention is drawn to methods of structural framework identification.

e) and f) One of skill in the art would not be able to practice the said invention because there is no guidance as to how to engineer a protein using said method. One of skill in the art could, in the best case scenario, identify proteins suitable for further modification.

f) The skill of those in the art of molecular biology is high. However, absent further guidance, one of skill in the art could not engineer proteins using said method.

g) The prior art indicates that it is possible to submit query sequences in order to compare similarities and difference in hopes of identifying useful compounds. However, query comparison to a know sequence will not produce or engineer a protein.

Claims 1-30 are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and dependent claims recite “a method of protein engineering.” However, the steps outlined in the independent claims do not lead to an engineered protein. At best, the method determines structural framework similarities to a query sequence.

Claims 11-13 recite “a protein with greater stability than the sample” or “protein capable of exhibiting a function similar to or inhibitory” of the sample. This, however, is not possible with out actual testing and comparison steps that would allow one to establish stability or similarity.

Claims 29 and 30 contain the trademark/trade names VECTRIX and POSTVEC. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is

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used to identify/describe a computer program of the instant invention and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-14, 16-19, 27, and 28 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 97/41526 (Wilson et al.).

Wilson et al. disclose identification of molecules which bind an EPO receptor and act as an EPO mimetic (page 3, lines 1-7). The computer based method involves methods for

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identifying compounds having a desired structure using three-dimensional coordinates of a subset of the atoms in a peptide (page 6, lines 15-17). Three-dimensional database programs, such as MACCS-3D and Sybyl/3DB, also used in the instant invention, are used to identify molecules bearing the desired pharmacophore (page 8, lines 1-4). The input for each entry is represented by coordinates such as distance coordinates which are utilized to locate the best hits (see coordinate listings, pages 74). Furthermore, Wilson et al. are particularly interested in the cytokine EPO, as the complex contains a D1 region with a two conserved disulfide bridges linking Cys²⁸ to Cys³⁸ and Cys⁶⁷ to Cys⁸³ (page 13, lines 19-27), meeting the limitations of claims 3-5 and others requiring cytokines with cysteine rich domains. The desired outcome of the invention disclosed by Wilson et al. is to design small molecule mimetics that are smaller than the natural hormone that can act as to produce appropriate biological responses (page 25, lines 10-25).

Claims 1, 7, 16, 17, 27 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,752,019 (Rigoutsos et al.).

The invention of Rigoutsos et al. relates to a computer system and method for recognizing those molecules in a database of one or more molecules which contain substructures in common with one or more test molecules. The data consists of protein structures represented by three-dimensional coordinates (see columns 1 and 2). Within the framework of this method, molecules are assessed by structure insertion, structure membership, similarity searches, and super-structure searches (column 2, lines 46-65). Attributes of molecules include data structures that are associated with vector information pertaining to each molecule in the database, wherein searches are conducted by clique detection (see column 8).

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Claims 1-13, 16, 18, 27, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,853,871 (Pantoliano et al.).

Pantoliano et al. disclose a computer-based method that evaluates the structure of a protein to thereby identify sites in the protein molecule at which the natural amino acid residues can be replaced with cysteine residues in order to permit the formation of a potentially stabilizing disulfide bond (see abstract). The method involves database query to determine 3-D similarities to known proteins, finding likely candidates, ranking candidates in terms of most stabilizing (see column 9, 4th step). Furthermore, the invention involves assessment of disulfide bond formation in effort to identify potential substitution residues (cysteine substitution) for development of stabilized proteins (columns 15 and 16). The method further involves examination of three-dimensional configurations and intersulfur distances of the disulfide bridges, the pyramid formed from the nitrogen, alpha carbon, beta carbon, and carbonyl carbon of the individual cysteines (see column 15, lines 15-20 and Table 1).

Claims 1, 2, 7, 16, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Lauri et al. (Journal of Computer Aided Molecular Design, Vol. 8 (1994) pages 51-66).

Lauri et al. disclose the computer program, CAVEAT, which was devised to facilitate structure-based design of enzyme inhibitors and related biologically active molecules. The program may be used for any such project attempting to identify proteins that are similar to query proteins. The CAVEAT search engine is designed to retrieve from a database of 3D structure molecules with specific bonds that match a vector relationship specified in the query. The geometrical attributes of the bonds, rather than their chemical or electronic character, are the primary issue. The representation of the specific bonds in the database structures as vectors, and

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the pre-organization of a database around pre-computed pairs of such vectors (vector pairs) are the key features of the CAVEAT search process (page 53, 1st paragraph). Furthermore, the choice of vector pairs may comprise a variety of sources, such as a database comprising vector pairs of substituents of cyclic or polycyclic molecules (page 54, 2nd paragraph). Claims 29 and 30, while incorporating the names VECTRIX and POSTVEC, are not different from the program CAVEAT and are also rejected. The programs, regardless of the name, are the same.

Claims 18 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,643,564 (Hamaguchi et al.).

Hamaguchi et al. disclose modified cytokines which insure migration to the liver (abstract). Claims 18 and 19 simply recite a modified framework protein product, which is clearly anticipated by the modified cytokines of Hamaguchi et al. The method of the claims does not materially affect the product.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10:00am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

December 14, 2002

Lori A. Clow, Ph.D.

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Lori A. Clow

MKZ
MARY K. ZEMAN
PRIMARY EXAMINER
1631